REMARKS

Applicants are filing this Response After Final Action because Applicants believe that all claims now presented are in condition for allowance. In any event entry of this response will place the application in better form for appeal. Applicants have raised no new issues and added no new matter. Finally the arguments presented herein are in direct response to points raised by the Examiner in the last office action and Applicants could not have filed their response at an earlier date.

The Examiner argues that pursuant to 35 USC 103 Claims 1 through 11 are obvious to a person skilled in the art at the time of the invention in the view of the combination of the USLU, WATANABE, BLACK and TRITTHART referencess. Applicants maintain that the invention as covered in claims 1 through 11 is still inventive and the invention is neither disclosed nor suggested by any of the four cited references, taken individually or in combination.

The presently claimed pharmaceutical formulations of claims 1 through 11 comprises the following ingredients:

an oral sachet formulation,

polymer coated alendronate <u>microparticles,</u>

therapeutically effective amount of alginic acid or sodium alginate for the purpose of preventing esophageal irritation caused by the alendronate,

sucrose and sodium saccharine as sweeteners,

microcrystalline cellulose as diluent, and

colloidal silica as a lubricant

Applicants emphasize that in particular the presently claimed formulations include microparticles of alendronate coated with a polymer soluble at a gastric pH of 1 to 4, but insoluble at a salivary pH of 6 to 7.5. Applicants assert that such coated microparticles of alendronate are novel and that the combination of these cited references would not lead one skilled in the art to prepare same.

Applicants' use of the term "microparticles" to define the particle size of the polymer-coated alendronate according to the presently claimed formulations serves to sharply distinguish the presently claimed formulations over each of the USLU, WATANABE, BLACK and TRITTHART referencess, as well as over the combination of these references notwithstanding the Examiner's comments on page 12, first full paragraph of the office action stating that Applicants fail to offer a special definition of microparticles or a preferred particle size range. Applicants submit that they need include no such special definition or preferred particle size range to distinguish over the prior art references.

USLU discloses a biphosphonate and alginate in granular form. It is common general knowledge to the person skilled in the art that a granular form is very different from a microparticle form. It is textbook or dictionary information that can be obtained by a simple search. The respective definitions for granules and microparticles taken from online dictionaries are attached to this Response. As can be seen from the cited documents, "microparticles" according to Wikipedia are defined as particles having a size between 0.5 μm to 0.5 mm whereas the "granules" are defined according to the Free Dictionary On Line as particles having a size between 2 and 4 mm diameter. Thus even the largest microparticles are still four times smaller than the smallest granules. Since neither USLU nor any of the other three prior art references discloses or suggests microparticles of alendronate, either coated or uncoated, the combination of the four cited references does not lead to the presently claimed invention.

The Examiner states that WATANABE *et al discloses* pharmaceutical compositions containing bisphosphonates for oral use that use the polymer as a coating to improve taste masking, moisture resistance as well as improving solubility and adsorption. But as Applicants stated in their previous responses, WATANABE et al does not disclose microparticles of alendronate or of any other bisphosphonate, does not disclose combining alginic acid or sodium alginate with alendronate for any purpose, let alone to prevent esophageal irritation caused by alendronate and provides no motivation for one skilled in the art to either employ alendronate microparticles, to

coat the alendronate microparticles with a polymer such as EUDRAGIT E100 or to combine the coated microparticles with alginic acid/sodium alginate all to prevent esophageal irritation caused by the prior art compositions containing alendronate. The purpose for coating alendronate for the Applicants' presently claimed invention to prevent esophageal irritation is neither disclosed nor suggested in WATANABE et al. Furthermore none of the USLU, BLACK and TRITTHART referencess even suggests preparing alendronate microparticles or coating the alendronate microparticles with a polymer such as EUDRAGIT E100 for any purpose at all, let alone to prevent esophageal irritation.

The Examiner, in response to Applicants' previous arguments, that the combination of the four prior art references fails to lead one skilled in the art to the presently claimed invention, asserts that USLU discloses the use of alginate in combination with particles of alendronate to prevent esophageal reflux. However, according to USLU the particles of alendronate are uncoated granules, not polymer-coated alendronate microparticles. Applicants use alginate/alginic acid in combination with the polymer coated microparticles of the alendronate for preventing esophageal irritation, which is not disclosed or suggested in any of the cited prior art references, taken individually or in combination.

Additionally, even though the use of sweeteners is cited in TRITTHART, the use of microcrystalline cellulose as a diluent and colloidal silica as a lubricant is not disclosed.

As a result, the presently claimed invention (Claims 1-11) includes an oral formulation of alendronate for overcoming the side effects specifically for preventing esophageal irritation. All of the features of this invention namely sachet formulation, polymer coating of alendronate in microparticle form and the use of therapeutically effective amount alginate or alginic acid altogether are for minimizing the side effects of alendronate.

Therefore, Applicants believe that the documents cited by the Examiner can not be a motivation for this invention even if they are combined.

Applicants believe that all claims now in the application are allowable over the cited combination of prior art references and Applicants earnestly solicit a response to that effect.

K.F. Ross P.C.

/Jonathan Myers/

By: Jonathan Myers, 26,963
Attorney for Applicant

08 December 2009
5683 Riverdale Avenue Box 900
Bronx, NY 10471-0900
Cust. No.: 535
Tel: 718 884-6600
Fax: 718 601-1099
Email: *email@kfrpc.com*
Enclosures: excerpts from on line dictionaries defining microparticles and granular particles
ge/